IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Hermann Bujard, and Manfred Gossen

Serial No.: (Continuation application of Serial No. 09/489,777)

Filed: August 3, 2001 (herewith)

For: *TETRACYCLINE-INDUCIBLE TRANSCRIPTIONAL INHIBITOR FUSION PROTEINS (as amended)*

Attorney Docket No.: BBI-009C6CNDVCN

Group Art Unit:

Examiner:

Commissioner for Patents
Box Patent Application
Washington, D.C. 20231

CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: August 3, 2001 Mailing Label Number: EL 916 823 640 US

I hereby certify that this Preliminary Amendment is being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Assistant Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

Viriato L Cardoso
Name of Person Mailing Paper

Viriato L Cardoso
Signature of Person Mailing Paper

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination of the above-identified application, please amend the application as follows:

In the Specification:

Please replace the title beginning at page 1, line 3 and at page 97, line 2, with the following new title:

--TETRACYCLINE-INDUCIBLE TRANSCRIPTIONAL INHIBITOR FUSION PROTEINS--

Please replace the paragraph beginning at page 1, line 6, under the heading "Related Applications", with the following rewritten paragraph:

--This application is a continuation of U.S. Serial No. 09/489,777, filed January 24, 2000, pending, which is a divisional of U.S. Serial No. 09/162,184, filed September 28, 1998, now U.S. Patent No. 6,136,954, which is a continuation of U.S. Serial No. 08/485,978, filed June 7, 1995, now U.S. Patent No. 5,814,618, which is a continuation-in-part of U.S. Serial No. 08/383,754, filed February 3, 1995, now U.S. Patent No. 5,789,156, which is a continuation-in-part of U.S. Serial No. 08/275,876, filed July 15, 1994, now U.S. Patent No. 5,654,168, which is a continuation-in-part of U.S. Serial No. 08/270,637, filed July 1, 1994, now abandoned. U.S. Serial No. 08/485,978 is also a continuation-in-part of U.S. Serial No. 08/260,452, filed June 14, 1994, now U.S. Patent No. 5,650,298, which is a continuation-in-part of U.S. Serial No. 08/076,327, filed June 14, 1993, now abandoned. U.S. Serial No. 08/485,978 is also a continuation-in-part of U.S. Serial No.08/076,726, filed June 14, 1993, now U.S. Patent No. 5,464,758. The entire contents of each of these applications are incorporated herein by reference.

In the claims:

Please cancel claim 1 without prejudice, and add new claims 32-51 as follows:

--32. **(NEW)** A fusion protein which inhibits transcription in eukaryotic cells, the fusion protein comprising a first polypeptide which binds to *tet* operator sequences, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells.

33. **(NEW)** The protein of claim 32, wherein the first polypeptide binds to *tet* operator sequences in the absence but not the presence of tetracycline or a tetracycline analogue.

34. **(NEW)** The protein of claim 33, wherein the first polypeptide is a Tet repressor.

35. **(NEW)** The protein of claim 34, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO: 17.

36. **(NEW)** The protein of claim 32, wherein the first polypeptide binds to *tet* operator sequences in the presence but not the absence of tetracycline or a tetracycline analogue.

37. **(NEW)** The protein of claim 36, wherein the first polypeptide is a mutated Tet repressor.

38. **(NEW)** The protein of claim 37, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

39. **(NEW)** The protein of claim 37, wherein the mutated Tet repressor has at least one amino acid addition or deletion compared to a wild-type Tet repressor.

40. **(NEW)** The protein of claim 37, wherein the mutated Tet repressor has an amino acid substitution at at least one amino acid position corresponding to an amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102 of a wild-type Tn10-derived Tet repressor amino acid sequence.

41. **(NEW)** The protein of claim 37, wherein the mutated Tet repressor comprises an amino acid sequence shown in SEQ ID NO: 19.

42. **(NEW)** The protein of claim 34, wherein the second polypeptide comprises a transcription silencer domain of a v-erbA oncogene product.

43. **(NEW)** The protein of claim 42, wherein the second polypeptide comprises an amino acid sequence shown in SEQ ID NO: 23.

44. **(NEW)** The protein of claim 37, wherein the second polypeptide comprises a transcription silencer domain of a v-erbA oncogene product.

45. **(NEW)** The protein of claim 42, wherein the second polypeptide comprises an amino acid sequence shown in SEQ ID NO: 23.

46. **(NEW)** The protein of claim 34, wherein the second polypeptide comprises a transcription silencer domain of a Drosophila Kruppel protein.

47. **(NEW)** The protein of claim 46, wherein the second polypeptide comprises an amino acid sequence shown in SEQ ID NO: 21.

48. **(NEW)** The protein of claim 37, wherein the second polypeptide comprises a transcription silencer domain of a Drosophila Kruppel protein.

49. **(NEW)** The protein of claim 48, wherein the second polypeptide comprises an amino acid sequence shown in SEQ ID NO: 21.

50. **(NEW)** The protein of claim 34, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SFI, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

51. **(NEW)** The protein of claim 37, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SFI, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

REMARKS

Claim 1 was originally filed in the application. Claim 1 has been canceled without prejudice. New claims 32-51 have been added. Accordingly, claims 32-51 are currently pending.

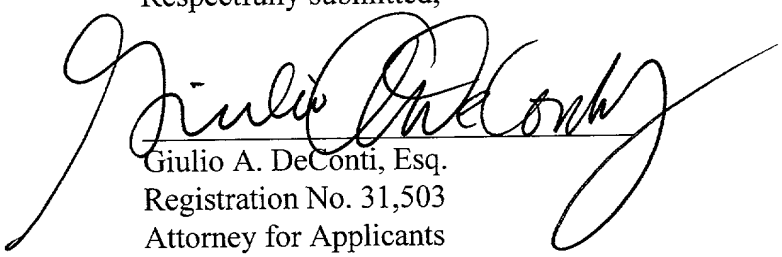
The title has been amended to more accurately reflect the subject being claimed in the application. The specification has been amended to update and correct the priority claim. Applicants submit herewith a "VERSION WITH MARKINGS TO SHOW CHANGES MADE", set forth as Appendix A, which shows the specific amendments made to the title and the specification. New claims 32-51 are directed to transcriptional inhibitor fusion proteins. Support for these claims can be found in the specification at, for example, pages 30-34.

No new matter has been added by way of the amendments to the specification or the new claims. Applicants respectfully request that these amendments be entered.

SUMMARY

All pending claims are believed to be in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



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Dated: August 3, 2001

APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The title beginning at page 1, line 3 and at page 97, line 2, has been amended as follows:

~~METHODS FOR REGULATING GENE EXPRESSION~~ TETRACYCLINE-INDUCIBLE TRANSCRIPTIONAL INHIBITOR FUSION PROTEINS

The paragraph beginning at page 1, line 6, under the heading "Related Applications", has been amended as follows:

This application is a continuation of U.S. Serial No. 09/489,777, filed January 24, 2000, pending, which is a divisional of U.S. Serial No. 09/162,184, filed September 28, 1998, now U.S. Patent No. 6,136,954, which is a continuation of U.S. Serial No. 08/485,978, filed June 7, 1995, now U.S. Patent No. 5,814,618, which is a continuation-in-part of U.S. Serial No. 08/383,754, filed February 3, 1995, now U.S. Patent No. 5,789,156, which is a continuation-in-part of U.S. Serial No. 08/275,876, filed July 15, 1994, now U.S. Patent No. 5,654,168, which is a continuation-in-part of U.S. Serial No. 08/270,637, filed July 1, 1994, now abandoned. U.S. Serial No. 08/485,978 is also a continuation-in-part of U.S. Serial No. 08/260,452, filed June 14, 1994, now U.S. Patent No. 5,650,298, which is a continuation-in-part of U.S. Serial No. 08/076,327, filed June 14, 1993, now abandoned. U.S. Serial No. 08/485,978 is also a continuation-in-part of U.S. Serial No.08/076,726, filed June 14, 1993, now U.S. Patent No. 5,464,758. ~~This application is also a continuation-in-part of U.S. Serial No. 08/275,876, filed July 15, 1994, which is a continuation-in-part of U.S. Serial No. 08/270,637, filed July 1, 1994, now abandoned. This application is also a continution-in-part of U.S. Serial No. 08/260,452, filed June 14, 1994, which is a continuation-in-part of U.S. Serial No. 08/076,327, filed June 14, 1993, now abandoned. This application is also a continution-~~

~~in part of U.S. Serial No. 08/076,726, filed June 14, 1993.~~ The entire contents of each of these applications are incorporated herein by reference.